Investigation of the binding mode and binding interactions of ML300-derivatives as potential anti-SARS-CoV-2 agents through molecular docking calculations

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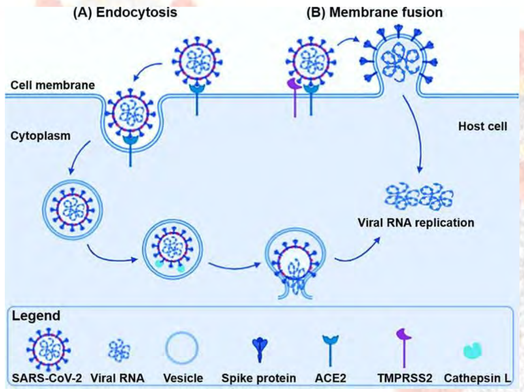
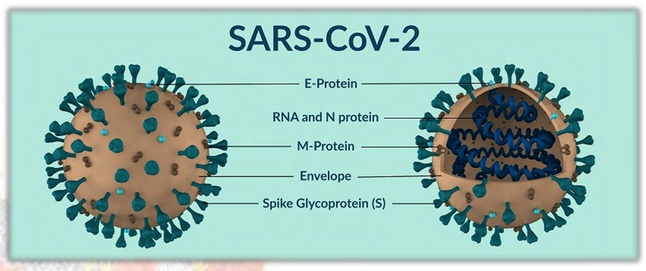
Introduction

▪ The main protease (M-Pro)

Chymotrypsin (3C)-like protease:
The most characteristic drug targets in coronavirus



https://journals.plos.org/plospathogens/article?id=10.1371/journal.ppat.1009013

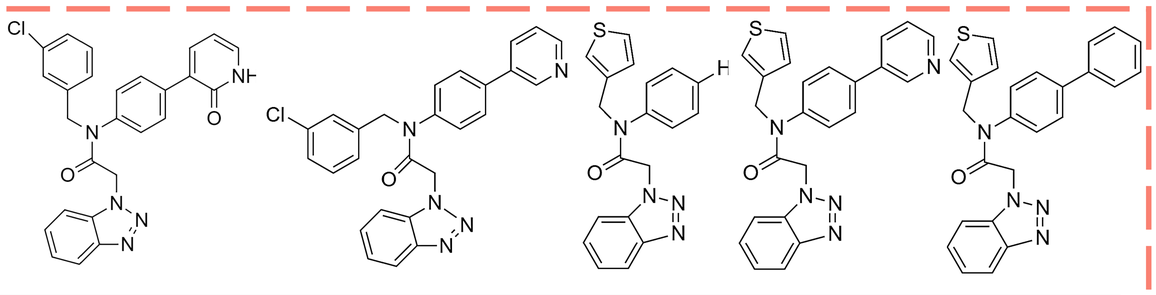


https://www.nsm.or.th/other-service/664-online-science/knowledge-inventory/sci-article/sci-article-science-museum/4649-sars-cov-2.html

A cysteine protease with an unconventional Cys catalytic residue, plays an essential role in coronavirus replication and transcription

SARS-CoV-2 main protease has been identified as a promising target for COVID-19 drug development.

Material and Methods



Cpd.	1	2	3	4	5
IC_{50} (μM)	0.66	0.25	19.73	0.93	16.82

https://doi.org/10.1021/acs.jmedchem.1c00598

Full optimized

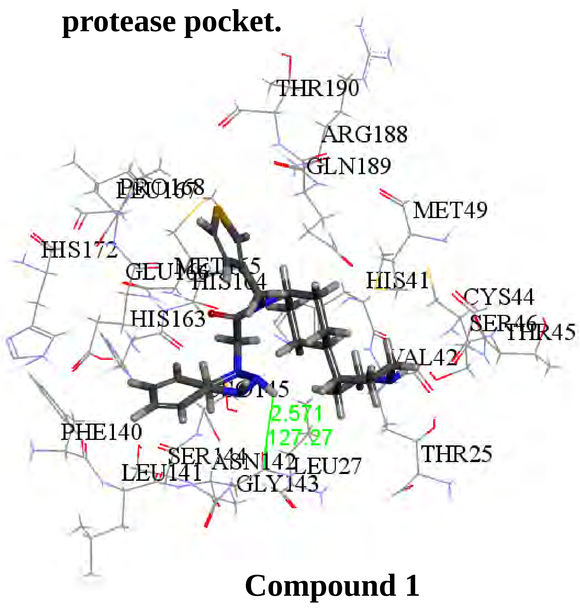
ML300-derivatives were built by Gaussview 5.08 program and were optimized by M062X/6-31G (d,p) method using Gaussian09 program.

Molecular docking calculations

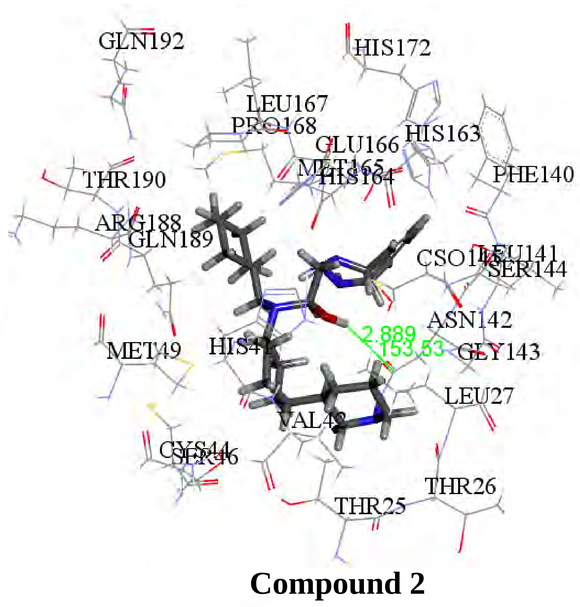
ML300-derivatives were docked to SARS-CoV-2 (PDB code : 7P51) domain by Glide program.

Results

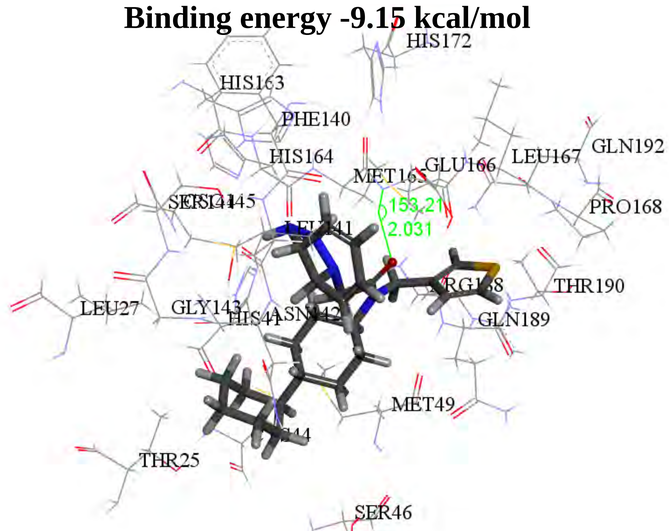
❑ **The binding mode and binding interaction of compounds in SARS-CoV-2 main protease pocket.**



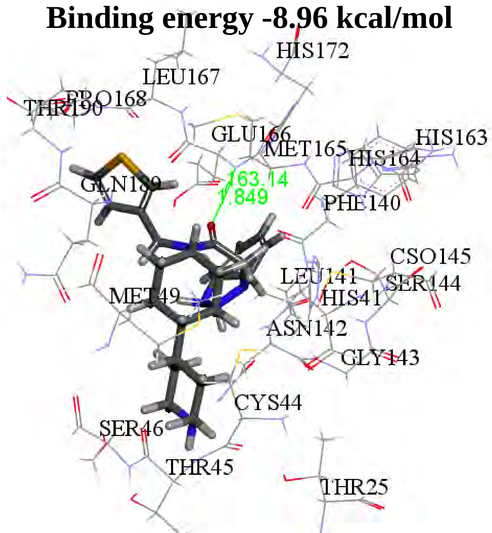
Compound 1
Binding energy -9.15 kcal/mol



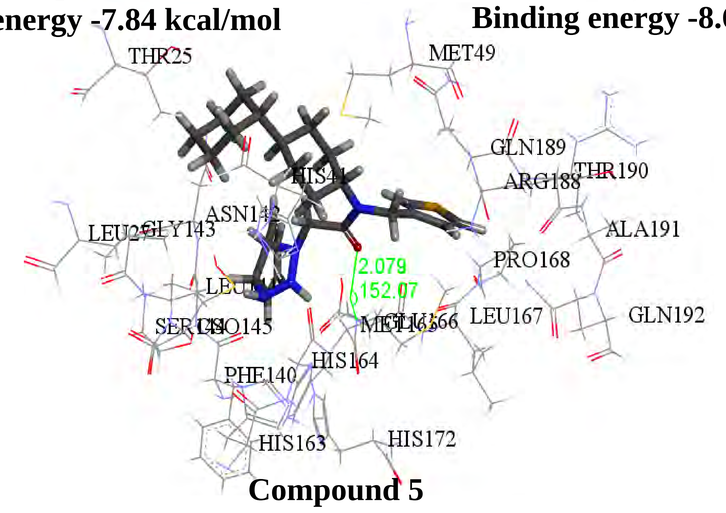
Compound 2
Binding energy -8.96 kcal/mol



Compound 3
Binding energy -7.84 kcal/mol



Compound 4
Binding energy -8.60 kcal/mol



Compound 5
Binding energy -8.95 kcal/mol

Conclusions

- ❑ The hydroxy group of all compounds interacted with Asn142 and Glu166 residues by hydrogen bond.
- ❑ ML300-derivatives have pi-sigma interactions between benzene ring with Gln189 residue and hydrophobic interactions with Met49, Met165 and Pro168 residues were found.
- ❑ Therefore, the obtained docking results of ML300-derivatives are beneficially informative for further rational design of new and potential inhibitors to combat COVID-19.

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